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10/810,527	03/26/2004	Kazuo Sugamura	671302-2007	9925

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EXAMINER	
LIETO, LOUIS D	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,527	SUGAMURA ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 1/11/2006 have been fully considered but they are not persuasive. The amendment has been entered. Claims 23-38 are pending. Claims 1-22 were canceled . The sections of 35 U.S.C. not included in this office action can be found in a previous office action. An action on the merits follows.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The rejection of claims 1-22 under 35 U.S.C. 112, first paragraph, because the specification does not enable the claims, is withdrawn because of applicant's cancellation of the claims.

Claims 23-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse with interstitial pneumonia or inflammatory bowel disease comprising a transgene, integrated into the mouse genome, which comprises an OX40L gene operably linked to a T-cell specific lck promoter that constitutively expresses OX40L in a T-cell specific manner, which causes the spontaneous onset of interstitial pneumonia or inflammatory bowel disease, and a method of making said mouse using pro-nuclear injection, does not reasonably provide enablement for any transgenic model mouse for interstitial pneumonia or inflammatory bowel disease comprising an expression vector having an OX40L

gene downstream of the T-cell specific lck promoter, wherein the expression vector is not integrated into the mouse genome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims encompass any transgenic model mouse for interstitial pneumonia or inflammatory bowel disease comprising an expression vector having an OX40L gene downstream of the T-cell specific lck promoter, which is not integrated into the mouse genome.

However, the specification only provides guidance on making a transgenic mouse, comprising a transgene, integrated into the mouse genome, which comprises an OX40L gene operably linked to a T-cell specific lck promoter, wherein the mouse constitutively expresses OX40L in a T-cell specific manner, The specification fails to provide adequate guidance and evidence for the production of any other transgenic mouse that can retain an expression vector in an episomal manner after injection into a mouse fertilized egg throughout the subsequent cell divisions that characterize mouse development. Further, the specification does not teach that an expression vector, which is not integrated into the mouse genome, can be passed onto to subsequent mouse generations through the meiotic events that are the hallmarks of sexual reproduction. The skilled artisan would not be able to predict how to make the claimed mouse in a manner commensurate in scope with the claim. Further, since the art of record does not provide any guidance on how to make transgenic mice that comprise an expression vector, which is not integrated into the mouse genome, the skilled practitioner would be reduced to guessing as to how to make such a mouse. This would require that the skilled practitioner engage in undue and extensive experimentation. Given the lack of guidance in the specification on how to make a

transgenic model mouse for interstitial pneumonia or inflammatory bowel disease comprising an expression vector having an OX40L gene downstream of the T-cell specific lck promoter, which is not integrated into the mouse genome and the lack of teachings in the art, the skilled practitioner would be unable to predict how to practice the claimed invention except as a transgenic mouse with interstitial pneumonia or inflammatory bowel disease comprising a transgene, integrated into the mouse genome, which comprises an OX40L gene operably linked to a T-cell specific lck promoter that constitutively expresses OX40L in a T-cell specific manner, which causes the spontaneous onset of interstitial pneumonia or inflammatory bowel disease, and a method of making said mouse using pro-nuclear injection, without undue and extensive experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is drawn to a transgenic mouse made by backcrossing a transgenic mouse with a C57BL/6 line mouse, which constantly expresses OX40L in T cells. It is unclear if the C57BL/6 line mouse or the result of the backcross constantly expresses OX40L in T cells. Therefore the metes and bounds cannot be determined.

Claim Rejections - 35 USC § 102

Claims 23-30 are rejected under 35 U.S.C. 102(a) as being anticipated by Ndhlovu[1] et al. {Ndhlovu[1] et al. (Sept.-01, 2001) J. of Immunology. 167:2991-2999}.

The reference of Ndhlovu[1] et al. lists several authors who are not listed as inventors on the instant application. Specifically, Lishomwa C. Ndhlovu, Naoto Ishii, and Takayuki Sato are not listed as inventors on the instant application.

Ndhlovu[1] et al. provides guidance on an OX40L transgenic mouse, constructed on the C57BL/6 background by using an lck promoter and constitutively expressing OX40L on T cells (Abstract; pg. 2992, col. 1). Wherein OX40-OX40L interactions are involved in graft-versus-host disease, inflammatory bowel disease, and asthma (pg. 2291, col.2 thru pg. 2992, col.1). Wherein said mice exhibited enhanced proliferative and cytokine responses to protein antigens, and showed a more severe progression of EAE and a greater mortality than wild-type mice (pg. 2993, col.2). The OX40L transgenic mouse inherently comprises the DNA sequence of SEQ ID NO:1, because the mouse of Ndhlovu[1] et al. is the same as the instantly claimed mouse. Thus, by teaching all the limitations of the claims as written, Ndhlovu[1] et al. anticipates the instant invention as claimed.

Applicant should note that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, the MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the

claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto, 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 23-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ndhlovu[2] et al. {Ndhlovu et al. (March 7, 2001) FASEB J., 15:A344}.

Ndhlovu[2] et al. provides guidance on an OX40L transgenic mouse. Wherein said mice exhibited a more severe progression of EAE than wild-type mice. The reference of Ndhlovu[2] et al. teaches an OX40L transgenic mouse that meets the limitations of the claims as evidenced by Ndhlovu[1] et al. {Ndhlovu et al. (Sept.-01, 2001) J. of Immunology. 167:2991-2999}. Ndhlovu[1] et al. discloses an OX40L transgenic mouse (Abstract; pg. 2992, col. 1). These mice inherently constantly express OX40L in T cells as evidenced by Ndhlovu[1] et al. The OX40L transgenic mouse inherently comprises the DNA sequence of SEQ ID NO:1, as evidenced by Ndhlovu[1] et al. Thus, by teaching all the limitations of the claims as written, Ndhlovu et al. anticipates the instant invention as claimed.

Applicant should note that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, the MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the

claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto, 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Claims 23-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Murata et al. {Murata et al. (2000) The 30th Annual Meeting of the Japanese Society of Immunology 1-B100-P0}.

Murata et al. provides guidance on an OX40L transgenic mouse, which constitutively expresses OX40L and was used for functional analyses. The reference of Murata et al. teaches an OX40L transgenic mouse that meets the limitations of the claims as evidenced by Ndhlovu[1] et al. {Ndhlovu et al. (Sept.-01, 2001) J. of Immunology. 167:2991-2999}. Ndhlovu[1] et al. discloses an OX40L transgenic mouse (Abstract; pg. 2992, col. 1). These mice inherently constantly express OX40L in T cells as evidenced by Ndhlovu[1] et al. The OX40L transgenic mouse inherently comprises the DNA sequence of SEQ ID NO:1, as evidenced by Ndhlovu[1] et al. Thus, by teaching all the limitations of the claims as written, Murata et al. anticipates the instant invention as claimed.

Applicant should note that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, the MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto, 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Claims 23-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Takayuki et al. {Takayuki et al. (2000) The 30th Annual Meeting of the Japanese Society of Immunology 2-A-013-P/O}.

Takayuki et al. provides guidance on an OX40L transgenic mouse, which displayed an enhanced inflammatory reaction in response to antigen treatment. The reference of Takayuki et al. teaches an OX40L transgenic mouse that meets the limitations of the claims as evidenced by Ndhlovu[1] et al. {Ndhlovu et al. (Sept.-01, 2001) J. of Immunology. 167:2991-2999}. Ndhlovu[1] et al. discloses an OX40L transgenic mouse (Abstract; pg. 2992, col. 1). These mice inherently constantly express OX40L in T cells as evidenced by Ndhlovu[1] et al. The OX40L transgenic mouse inherently comprises the DNA sequence of SEQ ID NO:1, as evidenced by Ndhlovu[1] et al. Thus, by teaching all the limitations of the claims as written, Takayuki et al. anticipates the instant invention as claimed.

Applicant should note that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, the MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto, 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Claims 23-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishii et al. {Ishii et al. (2000) The 30th Annual Meeting of the Japanese Society of Immunology 3-D-249-P/O}.

Ishii et al. provides guidance on an OX40L transgenic mouse, which displayed an enhanced inflammatory reaction in response to antigen treatment. The reference of Ishii et al. teaches an OX40L transgenic mouse that meets the limitations of the claims as evidenced by Ndhlovu[1] et al. {Ndhlovu et al. (Sept.-01, 2001) J. of Immunology. 167:2991-2999}. Ndhlovu[1] et al. discloses an OX40L transgenic mouse (Abstract; pg. 2992, col. 1). These mice inherently constantly express OX40L in T cells as evidenced by Ndhlovu[1] et al. The OX40L transgenic mouse inherently comprises the DNA sequence of SEQ ID NO:1, as evidenced by Ndhlovu[1] et al. Thus, by teaching all the limitations of the claims as written, Ishii et al. anticipates the instant invention as claimed.

Applicant should note that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, the MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto, 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Claims 23-30 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Ndhlovu[1] et al. { Ndhlovu[1] et al. (Sept.-01, 2001) J. of Immunology.

167:2991-2999}.describes that the claimed OX40L-transgenic mouse was made by K. Murata, N. Ishii, M. Nose, M. Yamada, L.C Ndhlovu, and K. Sugamura (pg. 2992, Materials and Methods: Mice). However, only K. Sugamura and K. Murata are listed as inventors on the instant patent application. The reference of Ndhlovu et al. indicates that other inventors invented the claimed invention.

Ndhlovu[1] et al. provides guidance on an OX40L transgenic mouse, constructed on the C57BL/6 background by using an lck promoter and constitutively expressing OX40L on T cells (Abstract; pg. 2992, col. 1). Wherein OX40-OX40L interactions are involved in graft-versus-host disease, inflammatory bowel disease, and asthma (pg. 2291, col.2 thru pg. 2992, col.1). Wherein said mice exhibited enhanced proliferative and cytokine responses to protein antigens, and showed a more severe progression of EAE and a greater mortality than wild-type mice (pg. 2993, col.2). The OX40L transgenic mouse inherently comprises the DNA sequence of SEQ ID NO:1, because the mouse of Ndhlovu[1] et al. is the same as the instantly claimed mouse. Thus, by teaching all the limitations of the claims as written, Ndhlovu[1] et al. anticipates the instant invention as claimed.

Applicant should note that "when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). Further, the MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto, 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Response to Arguments

Applicant's arguments filed 1/11/2006 have been fully considered but they are not persuasive. Applicant argues the prior 102 rejections have been resolved in view of the canceled and newly added claims. However, applicant has not explained how the newly added claims obviate the prior grounds of rejection. Since the claims currently under consideration are anticipated by the prior art of record, as set forth above, the rejections have been maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over {Murata et al. (2000) The 30th Annual Meeting of the Japanese Society of Immunology 1-B100-P0}, in view of Brinster et al. {Brinster et al. (1985) PNAS 82 :4438-4442}

Murata et al. provides guidance on an OX40L transgenic mouse, which constitutively expresses OX40L and was used for functional analyses. The reference of Murata et al. teaches an OX40L transgenic mouse that meets the limitations of the claims as evidenced by Ndhlovu[1] et al. {Ndhlovu et al. (Sept.-01, 2001) J. of Immunology. 167:2991-2999}. Ndhlovu[1] et al. discloses an OX40L transgenic mouse (Abstract; pg. 2992, col. 1). These mice inherently constantly express OX40L in T cells as evidenced by Ndhlovu[1] et al. The OX40L transgenic mouse

inherently comprises the DNA sequence of SEQ ID NO:1, as evidenced by Ndhlovu[1] et al. Murata et al. does not teach a method of making a transgenic mammal by pro-nuclear injection, or a method of screening for therapeutic compounds.

Brinster et al. supplements the guidance of Murata et al. by teaching a method of making a transgenic mouse by pro-nuclear injection (Abstract). Brinster et al. teaches the preparation of the DNA, and the steps required for successful microinjection (pg. 4438, col. 2).

Based on the guidance provided by Murata et al. on an OX40L transgenic mouse, which constitutively expresses OX40L and was used for functional analyses and the teachings of Brinster et al. on a method of making a transgenic mouse using pro-nuclear injection, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Murata et al. by making the mouse using the teachings of Brinster et al. Further, it would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to backcross the mice in order to obtain a pure transgenic strain, as many times as necessary, including twelve.

A practitioner in the art would have been motivated to make the mouse of Murata et al. using the techniques of Brinster et al., because the techniques were well known in the art and were validated methods for making transgenic mice. Further, the practitioner in the art would have been motivated to backcross the mice in order to obtain a pure transgenic strain, as many times as necessary, including twelve.

The person of ordinary skill in the art would have a reasonable expectation of success because using the method of Brinster et al., to make transgenic mice was standard practice in the art at the time of filing.

Response to Arguments

Applicant's arguments filed 1/11/2006 have been fully considered but they are not persuasive. Applicant argues the prior 103 rejection has been resolved in view of the canceled and newly added claims. However, applicant has not explained how the newly added claims obviate the prior rejection. Since the claims currently under consideration are anticipated by the prior art of record, as set forth above, the rejection has been maintained.

No claims allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier

communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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